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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER	
FORMAN, BETTY J	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 12/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/892,485	ISHIHARA ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 October 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-69* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

FINAL ACTION

Status of the Claims

1. This action is in response to papers filed 22 October 2004 in which claims 29, 34, 36-37, 41-42, 45-47, 54, 65-67 were amended. All of the amendments have been thoroughly reviewed and entered.

The previous rejections in the Office Action dated 22 June 2004 are withdrawn in view of the amendments. Applicant's arguments have been thoroughly reviewed but are deemed moot in view of the amendments, withdrawn rejections and new grounds for rejection. New grounds for rejection, necessitated by amendment are discussed.

Claims 29-69 are under prosecution.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 29-69 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The recitations "untransformed" and "gene expression patterns (1) to (4) is measured by determining the variation in the amount of gene transcription based on an electrophoretic pattern..." is added to the newly amended independent claims 29, 65-67, from which all other

pending claims depend. However, the specification fails to define or provide any disclosure to support such claim recitation.

Applicant points to page 11, lines 6-8 for support of the "untransformed". However, the cited passage merely teaches the cells are normal cells, cancer cells or may be genetically transformed. The specification does not teach or define the meets and bounds of the newly claimed "untransformed".

Applicant points to originally claims 7-10 and pages 15, 16 and 25-27 for support for the newly claimed "measured" gene expression pattern and determining "the variation in the amount" of gene transcription. The cited claims and passage teach electrophoresis and comparing intensity of fluorescent signals from the electrophoresis, the cited claims and passage do not teach measured gene expression patterns as newly claimed. Hence, the amendments introduce new matter into the specification.

MPEP 2163.06 notes "IF NEW MATTER IS ADDED TO THE CLAIMS, THE EXAMINER SHOULD REJECT THE CLAIMS UNDER 35 U.S.C. 112, FIRST PARAGRAPH - WRITTEN DESCRIPTION REQUIREMENT. *IN RE RASMUSSEN*, 650 F.2D 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application." MPEP 2163.06 further notes "WHEN AN AMENDMENT IS FILED IN REPLY TO AN OBJECTION OR REJECTION BASED ON 35 U.S.C. 112, FIRST PARAGRAPH, A STUDY OF THE ENTIRE APPLICATION IS OFTEN NECESSARY TO DETERMINE WHETHER OR NOT "NEW MATTER" IS INVOLVED. *APPLICANT SHOULD THEREFORE SPECIFICALLY POINT OUT THE SUPPORT FOR ANY AMENDMENTS MADE TO THE DISCLOSURE*" (emphasis added).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 29-41, 45-46, 48-49, 50-64, 65-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nilsson et al (U.S. Patent No. 5,578,445, issued 26 November 1996) in view of Falb (U.S. Patent No. 5,849,578, issued 15 December 1998).

Regarding Claim 29, Nilsson et al disclose a method for detecting an endocrine disrupting action of a test substance comprising culturing a cell sensitive to an endocrine hormone in the presence of the hormone (i.e. reference substance) and a test substance and detecting a gene expression pattern of said cell and comparing the expression pattern to the cell cultured in the absence of the test substance or the cell cultured in the absence of the hormone but the presence of the test substance or the cell cultured in the absence of the hormone and test substance wherein increased or decreased expression is indicative of endocrine disruption (Column 1, lines 39-Column 2, line 14) Furthermore, they provide specific embodiments wherein the reference sequence is estradiol (defined as a female hormone in the instant specification, page 10, lines 20-22) and the test substance is tamoxifen (Column 5, line 26-Column 6, line 23 and Claim 1). Nilsson et al does not teach untransformed cells and analysis of gene expression pattern by determining variation in gene expression based on an electrophoretic pattern of RNA or cDNA recovered from the cells.

However, these elements were well known and routinely practiced in the art at the time the claimed invention was made as taught by Falb.

Falb teaches a similar method for determining endocrine disrupting activity of a test substance comprising culturing normal cells (i.e. untransformed) in the presence and absence of the test substance and comparing gene expression to determine disruption (Column 74, lines 7-67). Furthermore, they provide specific preferred methods for expression comparison (sections 6.1.2 and 8.1) the methods comprising recovering the RNAs, reverse transcribing the

RNA, amplifying the transcription products and subjecting the amplified products to electrophoresis (Column 16, line 53-Column 18, line 65). Falb further teaches the RNA isolation, hybridization, subtraction, amplification and detection provides identification of genes differentially expressed is samples of interest (Column 16,lines 54-59). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the gene expression analysis of Nilsson et al with the RNA isolation, hybridization, subtraction, amplification and detection taught by Falb for the expected benefit of identifying sample-specific gene expression as desired in the art as taught by Falb (Column 16, lines 54-59).

Regarding Claim 30 Nilsson et al disclose the method wherein the expression pattern from (1) hormone with test substance is compared to (2) hormone without test substance (Column 6, lines 1-8).

Regarding Claim 31, Nilsson et al disclose the method wherein the expression pattern from (1) hormone with test substance is compared to (3) no hormone with test substance (Column 6, lines 1-8).

Regarding Claim 32, Nilsson et al disclose the method wherein the expression pattern from (1) hormone with test substance is compared to (2) hormone without test substance (3) no hormone with test substance (Column 6, lines 1-8).

Regarding Claim 33, Nilsson et al disclose the method wherein the expression pattern from (1) hormone with test substance is compared to (4) no hormone or test substance (Column 6, lines 1-8).

Regarding Claim 34, Nilsson et al disclose the method wherein the expression patterns are measured by determining the variation is the amount of gene expression i.e. protein expression regulated by gene expression (Column 3, lines 11-17).

Regarding Claims 35-40, Nilsson et al disclose a method for detecting an endocrine disrupting action of a test substance comprising culturing a cell sensitive to an endocrine

hormone in the presence of the hormone (i.e. reference substance) and a test substance and detecting a gene expression pattern of said cell and comparing the expression pattern to the cell cultured in the absence of the test substance or the cell cultured in the absence of the hormone but the presence of the test substance or the cell cultured in the absence of the hormone and test substance wherein increased or decreased expression is indicative of endocrine disruption (Column 1, lines 39-Column 2, line 14) Furthermore, they provide specific embodiments wherein the reference sequence is estradiol (defined as a female hormone in the instant specification, page 10, lines 20-22) and the test substance is tamoxifen (Column 5, line 26-Column 6, line 23 and Claim 1) wherein the expression patterns are measured by determining the variation is the amount of gene expression i.e. protein expression regulated by gene expression (Column 3, lines 11-17).

Nilsson does not teach determining gene expression by recovering RNA from the cells and comparing for each cell treatment the RNA or cDNA from the RNA from the treated cells to determining endocrine disruption.

However, gene expression via RNA hybridization comparisons were well known in the art at the time the claimed invention was made as taught by Falb.

Falb teaches a similar method for determining endocrine disrupting activity of a test substance comprising culturing cells in the presence and absence of the test substance and comparing gene expression to determine disruption (Column 73, line 45-Column 74, line 35). Furthermore, they provide specific preferred methods for expression comparison (sections 6.1.2 and 8.1) the methods comprising recovering the RNAs, reverse transcribing the RNA, amplifying the transcription products and subjecting the amplified products to electrophoresis (Column 16, line 53-Column 18, line 65). Falb further teaches the RNA isolation, hybridization, subtraction, amplification and detection provides identification of genes differentially expressed is samples of interest (Column 16,lines 54-59). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify

the gene expression analysis of Nilsson et al with the RNA isolation, hybridization, subtraction, amplification and detection taught by Falb for the expected benefit of identifying sample-specific gene expression as desired in the art as taught by Falb (Column 16, lines 54-59).

Regarding Claim 41, Nilsson et al disclose the method wherein gene expression patterns are measured by determining a variation in the amount of protein expressed between A, B, C or D (Column 3, lines 11-17 and Column 5, line 65-Column 6, line 8).

Regarding Claim 45, Nilsson et al disclose the method wherein disruption is determined by identifying that a different amount of protein is expressed in A compared to B, C, or D (Column 3, lines 11-54).

Regarding Claim 46, Nilsson et al disclose the method wherein gene expression patterns are measured by determining a variation in the amount of protein expressed between A, B, C or D wherein variation is indicative of disrupting activity (Column 3, lines 11-17 and Column 5, line 65-Column 6, line 8). Regarding Claims 48-49, 55 and 59-64, Nilsson et al disclose a method for detecting an endocrine disrupting action of a test substance comprising culturing a cell sensitive to an endocrine hormone in the presence of the hormone (i.e. reference substance) and a test substance and detecting a gene expression pattern of said cell and comparing the expression pattern to the cell cultured in the absence of the test substance or the cell cultured in the absence of the hormone but the presence of the test substance or the cell cultured in the absence of the hormone and test substance wherein increased or decreased expression is indicative of endocrine disruption (Column 1, lines 39-Column 2, line 14). Furthermore, they provide specific embodiments wherein the reference sequence is estradiol (defined as a female hormone in the instant specification, page 10, lines 20-22) and the test substance is tamoxifen (Column 5, line 26-Column 6, line 23 and Claim 1).

Nilsson et al teach method wherein endocrine disruption of a test substance is analyzed in various cell and tissues whereby effects of the test substance in the cells or tissues is analyzed (Column 2, lines 54-66) and useful as a tool for predicting effects of test substances

as drug candidates (Column 1, lines 11-30). Nilsson et al further teach the preferred embodiment evaluates any steroid hormone, thyroid hormone or glucocorticoid hormones (Column 3, lines 4-8). These teachings clearly suggest the method is applicable for any cell or tissue sensitive to any endocrine hormone. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the specific embodiments taught by Nilsson by analyzing any cells (e.g. nerve cells or germ cells or murine) for any endocrine hormone (e.g. androgen, testosterone, adrenal cortex hormone, cortisol, aldosterone, amino acid derivative hormone, T3, T4 or parathyroid hormone) for the expected benefit of studying the effects of candidate drugs in cells of interest for modification of clinically important endocrine hormones as suggested by Nilsson et al (Column 1, lines 11-30).

Regarding Claim 50, Nilsson et al disclose the method wherein the cell is a normal cell (Column 2, line 54-Column 3, line 3).

Regarding Claim 51, Nilsson et al disclose the method wherein the cell is a cancer cell (Column 5, line 26-45).

Regarding Claim 52, Nilsson et al disclose the method wherein the cell is a nonhuman cell as taught by contrast to their preferred embodiment wherein the cell is human (Column 2, lines 54-58).

Regarding Claim 53, Nilsson et al disclose the method wherein the cell is a human cell (Column 2, lines 54-58).

Regarding Claim 54, Nilsson et al disclose the method wherein the cell is not genetically engineered i.e. human cell lines MCF7 and ZR 75-1 (Column 5, lines 26-28).

Regarding Claim 56, Nilsson et al disclose the method wherein the cell is MCF7 (Column 5, lines 26-28).

Regarding Claim 57, Nilsson et al disclose the method wherein the hormone is a female hormone i.e. estradiol (defined as a female hormone in the instant specification, page 10, lines 20-22) (Column 5, lines 45-54).

Regarding Claim 58, Nilsson et al disclose the method wherein the hormone is estradiol (Column 5, lines 45-54).

Regarding Claim 65, Nilsson et al disclose a method for detecting an endocrine disrupting action of a test substance comprising culturing a cell which is not genetically engineered and which is sensitive to an endocrine hormone in the presence of the hormone (i.e. reference substance) and a test substance and detecting a gene expression pattern of said cell and comparing the expression pattern to the cell cultured in the absence of the test substance or the cell cultured in the absence of the hormone but the presence of the test substance or the cell cultured in the absence of the hormone and test substance wherein increased or decreased expression is indicative of endocrine disruption (Column 1, lines 39-Column 2, line 14) Furthermore, they provide specific embodiments wherein the reference sequence is estradiol (defined as a female hormone in the instant specification, page 10, lines 20-22) and the test substance is tamoxifen (Column 5, line 26-Column 6, line 23 and Claim 1).

Nilsson et al does not teach untransformed cells. However, comparison of gene expression between treated and untreated normal cells was well known and routinely practiced in the art at the time the claimed invention was made as taught by Falb.

Falb teaches a similar method for determining endocrine disrupting activity of a test substance comprising culturing normal cells (i.e. untransformed) in the presence and absence of the test substance and comparing gene expression to determine disruption (Column 74, lines 7-67). Furthermore, they provide specific preferred methods for expression comparison (sections 6.1.2 and 8.1) the methods comprising recovering the RNAs, reverse transcribing the RNA, amplifying the transcription products and subjecting the amplified products to electrophoresis (Column 16, line 53-Column 18, line 65). Falb further teaches the RNA isolation, hybridization, subtraction, amplification and detection provides identification of genes differentially expressed is samples of interest (Column 16,lines 54-59). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to

modify the gene expression analysis of Nilsson et al with the RNA isolation, hybridization, subtraction, amplification and detection taught by Falb for the expected benefit of identifying sample-specific gene expression as desired in the art as taught by Falb (Column 16, lines 54-59).

Regarding Claim 66, Nilsson et al disclose a method for detecting an endocrine disrupting action of a test substance comprising culturing a cell which is not genetically engineered and which is sensitive to an endocrine hormone in the presence of the hormone (i.e. reference substance) and a test substance and detecting a gene expression pattern of said cell and comparing the expression pattern to the cell cultured in the presence of the hormone and absence of the test substance wherein increased or decreased expression is indicative of endocrine disruption (Column 1, lines 39-Column 2, line 14) Furthermore, they provide specific embodiments wherein the reference sequence is estradiol (defined as a female hormone in the instant specification, page 10, lines 20-22) and the test substance is tamoxifen (Column 5, line 26-Column 6, line 23 and Claim 1).

Nilsson et al does not teach untransformed cells and analysis of gene expression pattern by determining variation in gene expression based on an electrophoretic pattern of RNA or cDNA recovered from the cells.

However, these elements were well known and routinely practiced in the art at the time the claimed invention was made as taught by Falb.

Falb teaches a similar method for determining endocrine disrupting activity of a test substance comprising culturing normal cells (i.e. untransformed) in the presence and absence of the test substance and comparing gene expression to determine disruption (Column 74, lines 7-67). Furthermore, they provide specific preferred methods for expression comparison (sections 6.1.2 and 8.1) the methods comprising recovering the RNAs, reverse transcribing the RNA, amplifying the transcription products and subjecting the amplified products to electrophoresis (Column 16, line 53-Column 18, line 65). Falb further teaches the RNA

isolation, hybridization, subtraction, amplification and detection provides identification of genes differentially expressed is samples of interest (Column 16,lines 54-59). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the gene expression analysis of Nilsson et al with the RNA isolation, hybridization, subtraction, amplification and detection taught by Falb for the expected benefit of identifying sample-specific gene expression as desired in the art as taught by Falb (Column 16, lines 54-59).

Regarding Claim 67, Nilsson et al disclose a method for detecting an endocrine disrupting action of a test substance comprising culturing a cell which is sensitive to an endocrine hormone in the presence of the hormone (i.e. reference substance) and a test substance and detecting a gene expression pattern of said cell and comparing the expression pattern to the cell cultured in the presence of the hormone but in the absence of the test substance wherein increased or decreased expression is indicative of endocrine disruption (Column 1, lines 39-Column 2, line 14). Furthermore, they provide specific embodiments wherein the reference sequence is estradiol (defined as a female hormone in the instant specification, page 10, lines 20-22) and the test substance is tamoxifen (Column 5, line 26-Column 6, line 23 and Claim 1).

Nilsson et al does not teach untransformed cells. However, comparison of gene expression between treated and untreated normal test cells was well known and routinely practiced in the art at the time the claimed invention was made as taught by Falb.

Falb teaches a similar method for determining endocrine disrupting activity of a test substance comprising culturing normal cells (i.e. untransformed) in the presence and absence of the test substance and comparing gene expression to determine disruption (Column 74, lines 7-67). Furthermore, they provide specific preferred methods for expression comparison (sections 6.1.2 and 8.1) the methods comprising recovering the RNAs, reverse transcribing the RNA, amplifying the transcription products and subjecting the amplified products to

electrophoresis (Column 16, line 53-Column 18, line 65). Falb further teaches the RNA isolation, hybridization, subtraction, amplification and detection provides identification of genes differentially expressed is samples of interest (Column 16,lines 54-59). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the gene expression analysis of Nilsson et al with the RNA isolation, hybridization, subtraction, amplification and detection taught by Falb for the expected benefit of identifying sample-specific gene expression as desired in the art as taught by Falb (Column 16, lines 54-59).

Regarding Claim 68, Nilsson et al disclose the method of Claim 29 wherein expression pattern from (1) is compared to (2), (3) and (4) (Column 1, lines 39-Column 2, line 14; Column 5, line 26-Column 6, line 23 and Claim 1).

Regarding Claim 69, Nilsson et al disclose the method of Claim 29 wherein expression pattern from (1) is compared to (2) and then the comparison is compared with (3) and (4) i.e. reading from the bottom up of the table found at Column 6, lines 1-5 (Column 1, lines 39-Column 2, line 14; Column 5, line 26-Column 6, line 23 and Claim 1).

6. Claims 42-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nilsson et al (U.S. Patent No. 5,578,445, issued 26 November 1996) in view of Falb (U.S. Patent No. 5,849,578, issued 15 December 1998) as applied to Claim 29 above and further in view of Horwitz et al (U.S. Patent No. 6,750,015, filed 21 March 2001)

Regarding Claims 42-44, Nilsson et al disclose a method for detecting an endocrine disrupting action of a test substance comprising culturing a cell sensitive to an endocrine hormone in the presence of the hormone (i.e. reference substance) and a test substance and

detecting a gene expression pattern of said cell and comparing the expression pattern to the cell cultured in the absence of the test substance or the cell cultured in the absence of the hormone but the presence of the test substance or the cell cultured in the absence of the hormone and test substance wherein increased or decreased expression is indicative of endocrine disruption (Column 1, lines 39-Column 2, line 14) wherein gene expression patterns are measured by determining a variation in the amount of protein expressed between A, B, C or D (Column 3, lines 11-17 and Column 5, line 65-Column 6, line 8). Nilsson et al do not teach electrophoresis, SDS-PAGE, two-dimensional electrophoresis to measure protein expression however measuring protein expression was well known in the art at the time the claimed invention was made as taught by Horwitz et al who teach a similar method for analyzing endocrine hormone responsive gene expression wherein the gene expression is determined by measuring proteins using electrophoresis e.g. SDS-PAGE (Column 49, line 55-Column 50, line 14). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the protein expression measuring of Nilsson et al by utilizing well known protein measurements e.g. electrophoresis, SDS-PAGE or two-dimensional electrophoresis because one of ordinary skill would have had reasonable expectation of success using well know techniques.

7. Claim 47 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nilsson et al (U.S. Patent No. 5,578,445, issued 26 November 1996) in view of Falb (U.S. Patent No. 5,849,578, issued 15 December 1998) as applied to Claim 29 above and further in view of Dharmesh et al (Proc. Natl. Acad. Sci, USA, 1993, 90: 11127-11131).

Regarding Claim 47, Nilsson et al disclose a method for detecting an endocrine disrupting action of a test substance comprising culturing a cell sensitive to an endocrine hormone in the presence of the hormone (i.e. reference substance) and a test substance and detecting a gene expression pattern of said cell and comparing the expression pattern to the cell cultured in the absence of the test substance or the cell cultured in the absence of the hormone but the presence of the test substance or the cell cultured in the absence of the hormone and test substance wherein increased or decreased expression is indicative of endocrine disruption (Column 1, lines 39-Column 2, line 14) wherein gene expression patterns are measured by determining a variation in the amount of protein expressed between A, B, C or D (Column 3, lines 11-17 and Column 5, line 65-Column 6, line 8) but they do not teach recovering glycosylated proteins to determine expression patterns.

However, Dharmesh et al teach a similar method for detecting endocrine disruption wherein they teach that half line of the glycoprotein lutropin and biological activity at the hormone receptor level are dramatically affected by glycosylation (Abstract). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the protein analysis of Nilsson et al by analyzing glycosylation at taught by Dharmesh et al based on the important biological effects of glycosylation as taught by Dharmesh et al (Abstract).

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

9. No claim is allowed.
10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (571) 272-0745. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is

a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

BJ Forman, Ph.D.
Primary Examiner
Art Unit: 1634
December 21, 2004